

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the present application:

Listing of Claims:

1-8. (Cancelled)

9. (Currently Amended) A screening method for substances that have a candidate antidiabetic substance, said method ~~a mechanism of pharmacological action similar to that of pioglitazone,~~ comprising the steps of:

bringing a candidate antidiabetic substance to be screened into contact with a target protein represented by the following (a) or (b), wherein said candidate substance is a substance that has not yet been determined to be an antidiabetic:

(a) a target protein consisting of the amino acid sequence represented by SEQ ID NO: 2 which is capable of interacting with a thiazolidine derivative selected from the group consisting of pioglitazone, rosiglitazone, trolitazone or ciglitazone; or

(b) a target protein consisting of an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO: 2 (i) with the addition of one or plural amino acids ~~and/or~~ or (ii) with the deletion, substitution, or insertion of one to thirty amino acids, wherein said target protein retains the capability to interact with a thiazolidine derivative selected from the group consisting of pioglitazone, rosiglitazone, trolitazone or ciglitazone; [[and]]

screening for the presence or absence of any interaction between the candidate antidiabetic substance and the target protein represented by (a) or (b); and

determining that the candidate antidiabetic substance has a pharmacological action similar to that of the thiazolidine derivative.

10-22. (Cancelled)

23. (Currently Amended) A screening method for ~~substances that have a candidate antidiabetic substance, said method a mechanism of pharmacological action similar to that of pioglitazone,~~ comprising the steps of:

bringing a candidate substance to be screened into contact with a target protein comprising the amino acid sequence represented by SEQ ID NO: 2 which is capable of interacting with a thiazolidine derivative selected from the group consisting of pioglitazone, rosiglitazone, trolitazone or ciglitazone, wherein said candidate substance is a substance that has not yet been determined to be an antidiabetic; [[and]]

screening for the presence or absence of any interaction between the candidate antidiabetic substance and the target protein; and

determining that the candidate antidiabetic substance has a pharmacological action similar to that of the thiazolidine derivative.

24. (Currently Amended) [[A]] The screening method according to claim 9, wherein said candidate substance is a low molecular weight compound.

25. **(Currently Amended)** **[[A]]** The screening method according to claim 9, wherein said candidate substance is a protein.

26. **(Currently Amended)** **[[A]]** The screening method according to claim 23, wherein said candidate substance is a low molecular weight compound.

27. **(Currently Amended)** **[[A]]** The screening method according to claim 23, wherein said candidate substance is a protein.

28. **(Currently Amended)** **[[A]]** The screening method according to claim 9, wherein said protein is immobilized on a substrate and said candidate substance is brought into contact with said immobilized protein in order to measure the capability of said candidate substance to interact with said protein.

29. **(Currently Amended)** **[[A]]** The screening method according to claim 23, wherein said protein is immobilized on a substrate and said candidate substance is brought into contact with said immobilized protein in order to measure the capability of said candidate substance to interact with said protein.

30. **(Previously Presented)** A screening method according to claim 28, wherein said substrate is a chip.

31. **(Currently Amended)** [[A]] The screening method according to claim 29, wherein said substrate is a chip.

32. **(Currently Amended)** [[A]] The screening method according to claim 9, wherein said thiazolidine derivative is pioglitazone.

33. **(Currently Amended)** [[A]] The screening method according to claim 23, wherein said thiazolidine derivative is pioglitazone.

34. **(Currently Amended)** [[A]] The screening method according to claim 32, wherein said screening is performed by surface plasmon resonance.

35. **(Currently Amended)** [[A]] The screening method according to claim 33, wherein said screening is performed by surface plasmon resonance.

36. **(Currently Amended)** [[A]] The screening method according to claim 9, wherein said protein is protein (b) and wherein said deletion, substitution, or insertion is of one to ten amino acids.

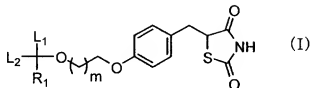
37. **(Currently Amended)** [[A]] The screening method according to claim 9, wherein said protein is protein (b) and wherein said deletion, substitution, or insertion is of one to five amino acids.

38. (Currently Amended) [[A]] The screening method according to claim 9, wherein said protein is said protein (a).

39. (Currently Amended) [[A]] The screening method according to claim 32, wherein said protein is said protein (a).

40-41. (Canceled)

42. (New) The screening method according to claim 9, wherein the candidate antidiabetic substance is represented by the general formula (I):

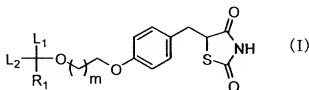


wherein R₁ is hydrogen, a C₁₋₁₀ alkyl group, a C₃₋₇ cycloalkyl group, a C₇₋₁₁ phenylalkyl group, a phenyl group, or a five- or six-membered heterocyclic ring comprising 1 or 2 heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur;

L₁ and L₂ are identical or different and are each independently hydrogen or a C₁₋₃ alkyl group or together to form a C₂₋₆ cycloalkyl group; and

m represents any integer from 1 to 5.

43. (New) The screening method according to claim 23, wherein said candidate antidiabetic substance is represented by the general formula (I):



wherein R_1 is hydrogen, a C_{1-10} alkyl group, a C_{3-7} cycloalkyl group, a C_{7-11} phenylalkyl group, a phenyl group, or a five- or six-membered heterocyclic ring comprising 1 or 2 heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur;

L_1 and L_2 are identical or different and are each independently hydrogen or a C_{1-3} alkyl group or together to form a C_{2-6} cycloalkyl group; and

m represents any integer from 1 to 5.

44. (New) A screening method for a candidate antidiabetic substance, said method comprising the steps of:

bringing a candidate antidiabetic substance to be screened into contact with a target protein represented by the following (a) or (b), wherein said candidate substance is a substance that has not yet been determined to be an antidiabetic:

(a) a target protein consisting of the amino acid sequence represented by SEQ ID

NO: 2 which is capable of interacting with a thiazolidine derivative selected from the group consisting of pioglitazone, rosiglitazone, troglitazone or ciglitazone; or

(b) a target protein consisting of an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO: 2, wherein the derived amino acid sequence has at least 90% homology with SEQ ID NO: 2 and retains the capability to interact with a thiazolidine derivative;

screening for the presence or absence of any interaction between the candidate antidiabetic substance and the target protein represented by (a) or (b); and

determining that the candidate antidiabetic substance has a pharmacological action similar to that of the thiazolidine derivative.